MEDICAL PROCEEDINGS

MEDIESE BYDRAES

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'n Suid-Afrikaanse Tydskrif vir die Bevordering van die Geneeskunde

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EDITORIAL · REDAKSIONEEL

WELLCOME RESEARCH TRAVEL GRANTS

To meet a need which, they were advised, was not covered by the existing systems of travelling fellowships, the Trustees of the Will of the late Sir Henry S. Wellcome (The Wellcome Trustees) instituted in 1955 a system of research travel grants* to enable workers on problems of human and animal medicine, and in related fields of experimental science, to pay short visits to other countries, so as to exchange views with colleagues with similar interests, to study or acquire new research techniques, or to attend scientific meetings dealing with the special subjects of their investigations. The duration of these awards may vary according to individual requirements, but will not normally exceed six months. The awards take the form of block grants towards the costs of travelling and in certain cases subsistence. For visits up to six weeks in duration the Trustees may be willing to provide the whole of the estimated cost but for longer visits they will usually be willing only to make a contribution to the total cost; the extent of this contribution will depend upon individual circumstances. Attendance at large international congresses does not normally come within the scope of Wellcome Research Travel Grants, but on occasion the Trustees may consider making a contribution towards the cost. Applications for Wellcome Research Travel Grants must be supported by the Vice-Chancellor of a University, by the Dean of the appropriate Faculty or College, or by the Head of a recognized re-

* See p. 181.

WELLCOME-REISTOELAES VIR NAVORSING

Om te voorsien in 'n behoefte wat, volgens die inligting wat tot hul beskikking gestel is, nie deur die huidige reistoelae-stelsels gedek word nie, het die Trustees van die testament van wyle sir Henry S. Wellcome (die Wellcome-trustees) in 1955 'n stelsel van navorsingsreistoelaes* ingestel sodat werkers op die gebied van menslike en dierlike geneeskunde, sowel as in die verwante sfere van eksperimentele wetenskap, kort besoeke aan ander lande kan aflê met die doel om gedagtes te wissel met kolleges wat dieselfde belange het, om nuwe navorsingstegnieke te bestudeer of baas te raak, of om wetenskaplike vergaderings by te woon waar die spesiale onderwerpe waarop hul navorsingswerk toegespits is, bespreek word. Die duur van hierdie toekennings wissel na gelang van individuele vereistes, maar in normale omstandighede sal dit nie ses maande oorskry nie. Die toekennings geskied in die vorm van globale toelaes vir die bestryding van reis- en, in sommige gevalle, ook verblyfkoste. In die geval van besoeke wat ses weke duur, sal die Trustees waarskynlik bereid wees om die hele beraamde koste te betaal, maar in die geval van langer besoeke sal hulle in die reël net gewillig wees om 'n bydrae tot die totale koste te doen. Die omvang van hierdie bydrae sal van individuele omstandighede afhang. Bywoning van die groot internasionale kongresse val normaalweg nie binne die bestek van die Wellcome-reistoelaes vir navorsing nie, maar die Trustees kan af en toe bereid wees om 'n bydrae tot die koste daarvan te oorweeg. Aansoeke om

* Bladsy 181.

search institution or department, who must be prepared to certify that the applicant is engaged in *bona fide* research, and that there are no local resources from which the cost of the visit could be met. Applications submitted without such support will not normally be considered.

In addition to these grants for visits of short duration, the Trustees are prepared in suitable cases to consider making block grants, for travelling expenses only, to workers in these fields of study who have been offered temporary paid research appointments (or research fellowships) for a year or more in Universities abroad. The general conditions governing these awards are similar to those of the short-term travel grants, and the applications must be similarly supported.

Enquiries about awards of either type should be addressed to the Deputy Scientific Secretary, The Wellcome Trust, 52 Queen Anne Street, London, W.1, from whom forms of application may be obtained.

'n Wellcome-reistoelae vir navorsing moet aanbeveel word deur die Onderkanselier van 'n universiteit, deur die Dekaan van die onderhawige Fakulteit of Kollege, of deur die Hoof van 'n erkende navorsingsinstituut of -departement, wat bereid moet wees om te sertifiseer dat die applikant *bona fide*-navorsingswerk doen, en dat daar geen plaaslike bronne bestaan waaruit die koste verbonde aan die besoek, bestry kan word nie. Aansoeke wat sonder so 'n aanbeveling ingedien word, sal in normale omstandighede nie oorweeg word nie.

Afgesien van hierdie toelaes vir kort besoeke is die Trustees ook bereid, in geskikte gevalle, om oorweging te verleen aan die toekenning van globale toelaes (slegs vir reiskoste) aan werkers op hierdie studiegebiede aan wie 'n tydelike, besoldigde navorsingsaanstelling (of 'n navorsingsbeurs) vir 'n jaar of langer aan 'n buitelandse universiteit toegestaan is. Die algemene voorwaardes wat op hierdie toekenning betrekking het, is soortgelyk aan dié vir korttermyn-reistoelaes, en aansoeke moet op 'n dergelike wyse aanbeveel word.

Navrae in verband met een of albei soorte toekennings moet gerig word aan die *Deputy Scientific Secretary, The Wellcome Trust,* Queen Anne-straat 52, Londen, W.1, by wie aansoekvorms verkrygbaar is.

ADRENOCORTICAL HORMONE AND CORTICOTROPHIN THERAPY

IN RELATION TO ANAESTHESIA AND SURGERY*

BERTRAM A. BRADLOW, M.D., M.R.C.P., M.R.C.P.E.
Johannesburg Hospital and Universiny of the Witwatersrand

New drugs bring new problems in the practice of medicine and the corticosteroids and corticotrophin are not exceptions to this rule.

When these drugs were first introduced it was felt that they prevented healing of wounds and lowered resistance to infection and therefore that they should be stopped before any surgery was attempted. Unfortunately these misconceptions are still held by many physicians and surgeons.

It was not an uncommon experience for a patient with rheumatoid arthritis who had been taking cortisone to have the drug 'tapered off' or stopped a month or two before an operation of election such as a herniorrhaphy, and the writer can recall at least two such cases which went into irreversible shock following anaesthesia for relatively minor procedures. Death was due to failure of the adrenal cortex resulting from adrenal suppression consequent on the use of corticosteroid therapy. Such shock can also occur in patients on corticosteroid treatment at the time of operation unless measures are taken, in these circumstances, to prevent such an eventuality.

It is known that prolonged administration of the adrenocortical hormones causes a decrease in size of the adrenal glands and even atrophy of the cortex. As a rule acute stress such as a surgical operation stimulates secretion of corticotrophin (ACTH) by the pituitary gland and this leads to increased secretion of adrenocortical hormones.[2] However, after continued use of adrenocortical hormones or corticotrophin, both pituitary and adrenocortical functions remain impaired for days, and even up to 18 months. The corticosteroids cause a loss in physiological sensitivity to ACTH.[1] There is also evidence that prolonged administration of ACTH may inhibit the release of corticotrophin by the pituitary and thus produce a lack of response to stress, including trauma and surgical operation. After pro-

* A paper read to a meeting of the Transvaal Branch of the South African Society of Anaesthetists on 27 January 1959.

longed administration of ACTH histological changes have been found in the pituitary similar to those described after administration of corticosteroids[3] and collapse may occur likewise in patients who have had prolonged treatment with ACTH before or up to the time of operation.

So far as is known, all the various hydrocortisone analogues such as prednisone, triamcinolone and dexamethasone are also capable of producing adrenocortical and pituitary suppression in the same way as cortisone or hydrocortisone.

It is proposed to deal with some of the important problems with which we are concerned, in the form of question and answer.

1. *What Proportion of People Develop Adrenocortical Insufficiency due to Surgery following on Corticosteroid or Corticotrophin Therapy?* Many thousands of patients who have received cortisone and other steroids or ACTH have been operated on and severe shock or collapse has been infrequent, so that most of such patients are able to stand the stress of operation without replacement therapy.[4] In the average case the weight of the adrenal gland has been shown to return to normal about 20 days after the use of cortisone has been stopped,[3] but adrenal atrophy may persist longer in certain subjects. This individual variation makes it difficult to be certain that adrenal cortical function is normal before operation.

2. *Can one Predict which Patients on Hormone (Steroid or ACTH) Therapy are Liable to Develop Post-Operative Collapse?* This can only be done to a limited extent and then only on clinical grounds. The features suggesting liability to adrenocortical insufficiency are 'moon face' and other features of Cushing's syndrome. In addition, patients who have had prolonged treatment or who are currently on treatment must be regarded as particularly liable to this complication. These types constitute an absolute indication for special pre- and post-operative care.

The assessment of adrenal cortical function by studying the fall in eosinophils following the injection of ACTH is not reliable, as a normal response to this test (or to a Soffer test of water excretion) does not necessarily indicate that the adrenal cortex is adequate to cope with operative stress.[1, 4] The increase in urinary excretion of 17-hydroxy-corticosteroids after an injection of ACTH is more reliable,[1, 2] especially in patients having long-term ACTH treatment, but the test is time-consuming and expensive. None of these tests is, of course, available in cases of emergency and therefore clinical indications are still the best.

3. *How Long must a Patient have been on Therapy and what Dosage must have been Given Before Adrenocortical Suppression Occurs?* Evidence exists that suppression may occur in some instances after 5 days of treatment with cortisone, although there is a great deal of individual variation.[3, 4] However, liability to adrenocortical failure is greatly increased when therapy has been prolonged over several months. The minimal dose of steroid that will significantly impair adrenal function is also not known, but theoretically any dose equalling or exceeding the daily physiological requirements may have this effect.[4] There is, however, no certainty that small daily doses are any less dangerous than larger ones.[4] A small dose of cortisone would be 20 mg. per day or less, and of prednisone 5 mg. per day. These facts are an indictment of the pharmaceutical firms who make 'shotgun' tablets containing small doses of steroids mixed with aspirin, tranquillizers or other drugs, as patients receiving this form of therapy are often unaware that they are having steroids. They may continue treatment for long periods and the doctor may be misled by the fact that the dose of hormone in each tablet is small.

4. *Does the Nature of the Operation Influence the Advent of Adrenocortical Failure?* There is no doubt that major operations and prolonged anaesthesia are more stress-producing than minor procedures, but fatalities have followed such a trivial procedure as a bilateral bunion operation.[4] Manipulation of a knee, grafting of an anal ulcer[1] and herniorrhaphy are other procedures which have been reported to have precipitated adrenal insufficiency. Thus special precautions should be taken, however trivial the procedure is thought to be.

5. *What is the Minimum Interval that must Elapse after Corticosteroid Therapy has been Stopped before the Suppressive Effect may be Considered to have been Abolished?* In some instances the duration of impaired pituitary adrenocortical function following the administration of prolonged and large doses of corticosteroids may last as long as a year or 18 months. This applies particularly to patients who manifest severe signs of hypercortisonism such as the Cushing's syndrome. However, as the present knowledge of how long adrenal suppression remains after withdrawal of the drug is unknown, it is safest to presume that any patient who has received corticosteroid therapy in significant dosage within 6 months should receive prophylactic treatment.[4] It is

probably safer to extent this period to 18 months when steroid therapy has lasted longer than 3 months.

6. *Does Corticotrophin or Corticosteroid Therapy Influence Wound Healing or Seriously Lower Resistance to Infection?* This is obviously the question which will be of concern to the surgeon. It may be said that serious interference with wound healing is rare unless the dosage is excessive (more than 150 mg. of cortisone daily) and prolonged, and protein intake is inadequate.[2] In 36 operations of various types done during treatment with either adrenocortical steroids or corticotrophin, wound healing and bone repair were uneventful.[2] There is also evidence that liability to infection is not increased with ordinary dosages.[2]

7. *How can Adrenal Insufficiency be Prevented?* It is first essential to enquire from the patient and his medical attendant whether corticosteroid or ACTH therapy has been used in the last 18 months, bearing in mind that steroids may be combined with ordinary analgesics, such as aspirin, in the same tablet.

Patients concurrently receiving treatment and those who have had significant amounts of hormone in the previous 12 to 18 months should be treated.

If the operation is to be prolonged or severe or if the patient has had a prolonged course of treatment with large doses, larger doses of steroid must be given than if the operation is a minor one, or the previous therapy with hormone was of short duration and of low dosage. In general, it is a better principle to give larger than smaller and possibly inadequate doses.

It is known that severe stress causes the adrenal glands to secrete the equivalent of 400 mg. of hydrocortisone daily[4, 5] and this must be taken into account in assessing dosage preoperatively.

For major cases as defined above, the Mayo Clinic workers[4, 5] recommend intramuscular cortisone acetate in doses of 200 mg. at 48, 24 and 2 hours before operation. Cortisone given orally before operation may be inadequate as its effects are of short duration (about 8 hours) and it does not create a depot of steroid. It must be remembered that intramuscular cortisone acetate is slowly absorbed and does not produce any noticeable effect for 6 to 12 hours, but its effects last for several days.

After operation 50 mg. cortisone acetate is given intramuscularly 12-hourly for 48 hours and then the patient either reverts to his normal maintenance dose or takes 25 mg. by mouth 2 or 3 times daily for a day or two, if he has stopped treatment before operation. It is seldom necessary to continue cortisone treatment for more than 3 to 4 days after operation.

Minor procedures usually require one half to two thirds of the above dosages.

Patients who are concurrently having ACTH should continue with their usual daily dose during the period of prophylactic treatment but should also be treated with the above regime.

8. *What Care Should be Given to a Patient who Requires an Emergency Operation or who has Inadvertently been Given an Anaesthetic without the Benefit of the Above Procedure?* These patients should at once be given 100 mg. of intravenous hydrocortisone sodium succinate (e.g. Solucortef or Venocort) and a further 200 mg. should be added to an intravenous drip. In addition 200 mg. of cortisone acetate should be given by intramuscular injection as soon as possible. The post-operative treatment is as already outlined above with intramuscular cortisone acetate and cortisone by mouth.

9. *What are the Signs of Adrenocortical Insufficiency and How is it Treated?* All patients who have a history of having had steroid treatment, regardless of whether or not they have received pre-operative treatment as outlined above, should be watched as though adrenal cortical insufficiency is expected especially during the first 24 hours after operation.[4] Pulse, blood pressure and temperature readings should be recorded at hourly intervals. Sudden circulatory collapse with a drop in blood pressure, increased pulse rate and very often a rise in temperature and sometimes coma are the signals to watch for and the occurrence of these signs should be regarded as a serious emergency.

Treatment is by means of intravenous hydrocortisone sodium succinate. The first dose should be 100 mg. intravenously and then 300–400 mg. can be given in an intravenous drip over the next 24 hours. In addition, 200 mg. of cortisone acetate should be given by intramuscular injection, so that a depot effect is produced. If the blood pressure does not rise almost immediately with this treatment, 4 mg. or more of noradrenaline should be added to the infusion bottle. It should be remembered that patients with adrenocortical failure are abnormally sensitive to drugs such as morphine and Omnopon, and these drugs should be used in small doses.

On recovery cortisone can be given by mouth in doses of 25 mg. 8-hourly for 2 to 3 days.

CONCLUSION

An attempt has been made to outline a practical policy for prevention of and, if necessary, treating adrenocortical insufficiency in patients who have had treatment with corticosteroids or corticotrophin.

It is hoped that this paper will lead to an increased awareness of the practical problems involved in the handling of such cases.

OPSOMMING

'n Poging is aangewend om die hooftrekke te beskrywe van 'n praktiese beleid vir die voorkoming en, indien nodig, die behandeling van adrenokortikale ontoereikendheid by pasiënte wat met kortikosteroïede of kortikotrofien behandel is.

Daar word gehoop dat hierdie referaat aanleiding sal gee tot 'n duideliker besef van die probleme wat deur die behandeling van sodanige pasiënte opgelewer word.

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LABOUR IN A CASE WITH ABDOMINAL WALL PARALYSIS

DAVID FRIEDBERG, M.B., B.CH., (RAND), M.R.C.O.G., F.C.O.G.(S.A.)*

Johannesburg

A new field in obstetrics has been opened by the use of abdominal decompression in labour (Heyns[1]).

This case report is significant in that in this patient nature was responsible for imitating in a sense what abdominal decompression does in labour. Because the abdominal musculature was severely paralysed, the wall offered almost no resistance to uterine movement during contractions.

Mrs. C. V. W., 34 years old, para 2, European, had her last menstrual period on 17 November 1954.

Estimated Date of Delivery: 24 August 1955.

She developed anterior poliomyelitis in 1949, at the age of 26 years. This resulted in a paralysis of both lower limbs and of the abdominal musculature.

Previous Obstetrical History. 1942: Spontaneous delivery of a live female infant, weighing 6 lb. 4 oz. During labour, she experienced severe pain and discomfort. Manual removal of the placenta. Labour lasted 20 hours.

1946: A 5 months' miscarriage, followed by dilatation and curettage of the uterus.

1947: Spontaneous delivery of a living female infant, weighing 7 lb. 1 oz. Manual removal of the placenta was done. She experienced pain and discomfort with this labour, which lasted 17 hours.

Present Pregnancy. The patient was well, she had had no headaches or visual disturbances. She did not suffer from morning sickness. *She was unable to defaecate or pass urine on her own.* She had to be given an enema, and was catheterized morning and evening, by a district Nursing Sister.

Ante-Natal Care. On 23 May she was examined for the first time. Her legs and abdominal wall were paralysed.

The knee and ankle jerks were absent.

The abdominal reflexes were absent.

No other significant findings were observed on general clinical examination.

Abdominal Examination. The abdominal musculature was paralysed. Estimated height of fundus—18 weeks. Vertex presentation.

Urine: Nothing abnormal was detected.

She was seen at 4-week intervals until the 28th week, and then at 2-week intervals until the 36th week, thereafter at weekly intervals until delivery.

The ante-natal period was uneventful.

CHARACTER AND CONDUCT OF LABOUR

The patient was admitted at 9.30 a.m. on 11 August 1955, with very slight contractions, occurring every half an hour. No pain was associated with contractions.

Rectal examination revealed that the cervix was well taken up, and the os one finger dilated.

Her general condition was satisfactory.

Abdominal Examination. The foetus was full term; head mobile; L.O.A. The foetal heart was heard beating at 136 per minute.

* Obstetrician and Gynaecologist.

Progress of Labour. She was given Oleum Ricini, 2 oz. orally, and an enema on admission.

Contractions were painless, and she had no discomfort.

11 a.m. Rectal examination: The cervical os was now 3 fingers dilated. She still suffered no discomfort or pain with her contractions. This was in contra-distinction to her 2 previous labours, where pain was a marked feature throughout the first stage.

Contractions now occurred every 2–3 minutes, fairly strongly, lasting 40 seconds.

12.15 p.m. She was still having painless contractions, lasting 40 seconds, every 2–3 minutes.

Abdominal Palpation: This confirmed the condition and position of the foetus (L.O.A.). The head was engaged.

Rectal Examination. The cervix was fully dilated. The presenting part (vertex) was half an inch below the ischial spines. The sagittal suture was in the antero-posterior diameter. The posterior fontanelle was directly anterior under the symphysis.

She was now fully dilated, but unable to bear down and expel the foetus. It was, therefore, decided to apply forceps.

12.30 p.m. She was given a general anaesthetic and, with an extremely easy pull, the foetus was delivered by means of Milne-Murray forceps.

The Third Stage of Labour. In view of the previous history of manual removals, the patient was given Ergotrate gr. 1/320 intravenously after the birth of the baby.

The placenta was delivered by simple expression, 3 minutes after the delivery of the foetus. The placenta and membranes were complete and healthy.

Duration of Labour:

First stage: 2 hours 45 minutes.
Second stage: 15 minutes.
Third stage: 3 minutes.
Total Duration of Labour: 3 hours 3 minutes.

Puerperium. She preferred to go home, and was discharged on the sixth day, to be nursed on district. Her stay in hospital had been uneventful. Her condition was satisfactory on discharge.

The infant cried lustily at birth. Weight, 7 lb. 3½ oz.

Post-Natal Examination (6 October 1955): The mother's condition was satisfactory, except for the paralysis. *Abdominal musculature*: Tone very poor.

The baby was on artificial feeds.

Vaginal Examination. Nothing abnormal was detected.

COMMENTARY

The main effect of uterine contraction in the first stage of labour is the rearrangement of the myometrium into a thick upper, and a thin lower segment. Almost certainly the stretched state of the amnion is the primary basis of cervical dilatation, and the stresses set up in the uterine wall with each contraction play only a secondary role. Unless the upper and lower segments differentiate as described above, the cervix will not dilate. Furthermore, unless the uterus changes shape, no myometrial shortening can occur. The consideration of the present case report is based on this latter fact.

During each first-stage contraction in this case, therefore, the uterus moved forward to a more spherical shape, with a minimum of resistance from the paralysed abdominal musculature. Muscle shortening of the isotonic type was thus freely possible. This is probably the explanation of her rapid first stage.

With the isometric type of myometrial contraction, i.e. when the uterus cannot change shape because of a rigid abdomen, the tension in the uterine wall is high. Presumably this high tension is transmitted to the sensorium and is there interpreted as the pain of labour.

In this case the parturient with her paretic abdominal wall felt no pain (because of the lack of isometric contractions) and, in consequence, had a short *painless* first stage.

What was an advantage in the first stage of labour had an adverse effect in the second stage. This patient clearly could not expel the foetus because the secondary powers were absent. For 200 years attempts have been made to explain expulsion of the foetus, and it has not been possible to substantiate the mechanism of axial pressure. It is now submitted that the uppermost part of the abdominal cavity becomes shut off from the lower regions during a contraction. If this is so, descent of the diaphragm during bearing down will increase the pressure of the chamber above the uterine fundus, and a pressure head will exist. On this basis, the foetus can be pushed down by axial pressure.

The upper chamber forms when, at the beginning of a painful contraction, the parturient tenses herself and her abdominal musculature. The uterus has moved forward as a result of the contraction, but is held firmly against the abdominal wall by this tightening. The only connexion between this upper chamber and the lower is the intestine which, however, is compressed tightly. In effect, therefore, the

abdominal cavity is no longer one chamber, but is divided into an upper part and an inferior part. The upper part is now in a position to have its pressure raised independently of the inferior portion. As the paralysed abdominal wall in this case was incapable of playing its part in effecting a sealed partition which is essential, the abdominal cavity had a uniform pressure throughout.

In the first stage, and possibly in the second, the effect of this mechanism was similar to what occurs during abdominal decompression. Decompression facilitates change of shape of the uterus from ellipsoid to spherical, and also has the effect of counteracting the adverse influence of a tense abdominal musculature.

It has been recorded in the history, that in this patient micturition and defaecation were possible only with enemata and catheterization. This reflects the degree of paralysis of the abdominal wall, and highlights the inadequacy of her expulsive powers in labour.

SUMMARY

A case is reported of a para-2 whose labours were normal in respect of pain and duration. An attack of poliomyelitis then paralysed her abdominal musculature.

She became pregnant again and went to term normally. Her labour, however, was very short (first stage 2¾ hours) and she suffered no pain or discomfort.

The findings in this case support the views of Heyns, who has attributed shortness of the first stage and reduction of pain during labour to relaxation of the abdominal wall, as produced by his decompression apparatus.

OPSOMMING

Verslag word gedoen oor 'n para-2 wie se bevalling normaal was vir sover dit pyn en duur betref. Haar buikspierstelsel is toe deur 'n aanval van poliomiëlitis verlam.

Sy het weer swanger geword en die einde van die tydperk op 'n normale manier bereik. Haar bevalling was egter van baie korte duur (die eerste stadium 2¾ uur), en sy het geen pyn of ongerief ondervind nie.

Die bevindings in hierdie geval staaf die sienswyses van Heyns wat die kortstondigheid van die eerste stadium en die vermindering van pyn tydens die bevalling toeskryf aan die verslapping van die buikwand, soos deur sy dekompressie-apparaat teweeggebring.

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THE DEVELOPMENT OF CARDIAC SURGERY

MALCOLM B. MCKENZIE, M.B., CH.B. (CAPE TOWN)

Department of Surgery, University of Cape Town and Groote Schuur Hospital, Observatory, C.P.

'The longer you look back, the further you can look forward,' said Sir Winston Churchill[1] in an address before the Royal College of Physicians in March 1944. By reviewing the past, gaps in our knowledge become clearly revealed and the struggles, the failures and the successes of our predecessors, which have led to our present state of knowledge, become more fully appreciated.

The recent successful development of techniques of extracorporeal oxygenation, first experimentally[2] and then clinically[3, 4] marks the opening of a new era in the history of surgery in South Africa, and it is fitting that at this time we should recall the work of those early pioneers of cardiac surgery who overcame prejudice and superstitution and who, by experimentation and clinical trial, developed the techniques on which our present-day methods are based. The story of their achievements constitutes a fascinating chapter in the history of medicine.

It is just 62 years since a suture was first successfully placed in the pulsating human heart by Rehn[5] and the possibilities of cardiac surgery were realized.

The physicians of antiquity believed with Hippocrates[6] that injuries of the heart were necessarily fatal:

> 'A severe wound of the bladder, of the brain, of the heart, of the diaphragm, of the small intestine, of the stomach and of the liver is deadly." (*Aphorisms*, VI, 18).

For nearly 20 centuries the aphorism of the Coan physician was undisputed and this view was endorsed throughout the ages by poet and physician alike, until the middle of the 18th century.

In the Bradshaw Lecture of 1919, Sir Charles Ballance[7] gave a number of delightful references to injuries of the heart mentioned in the classics. The description by Sophocles of the death of Ajax following his falling on his sword; Homer's account of the movement of a weapon in the heart (when Alkathous was

smitten by Idomeneus); the sudden death of Epanimondas at the battle of Mantinea, and of Sarpedon (wounded with a javelin by Patrohlas), immediately following the withdrawal of the weapons, are examples of the ancients' knowledge of cardiac wounds and their fatality. Aristotle[8] (384–322 B.C.) said: 'The heart alone of all viscera cannot withstand serious injury,' and Galen[9] (130–200 A.D.) describing wounds in gladiators, pointed out that if a ventricle was wounded these gladiators died soon, and especially so if the left ventricle was wounded. Fallopius[10] (1523–1562) asserted: 'Wounds of the heart are always followed by sudden death,' and Boerhaave[11] (1668–1738) stated: 'All wounds of the heart, deep enough to penetrate into either of its ventricles, are mortal.'

The validity of this widely held belief was questioned by Hollerius[12] as early as the sixteenth century, and in 1604 Cabriolanus[13] first described two cases in which, at autopsy, he found indisputable evidence of previous cardiac injury, unrelated to the cause of death. He concluded that the heart is able to suffer a non-fatal wound and this opinion was confirmed by Tourby[14] who, in 1642, reported the finding of a myocardial scar at autopsy on a man who had had a sword thrust in the chest 4 years before.

More than a century later, in 1761, Morgagni[15] first stressed the danger of compression of the heart from haemorrhage into the pericardial sac and in 1819 Romero[16] performed the first deliberate operation to drain the pericardium. Ten years later, Baron Larrey[17] (1829), Napoleon's surgeon, reported the successful management of a case of traumatic haemo-pericardium. He inserted a catheter through the stab wound and drained off three beakers of wine-coloured fluid. Following this success he wrote:

> 'We venture to say that practitioners . . . have without any real grounds, taken too grave a view of the effects of wounds of this fibroserous envelope and are perhaps open to the same reproach respecting certain wounds of the heart.'

It was not, however, until George Fischer[18] published his classic treatise on injuries of the heart in 1868, in which he recorded 452 cases with a 10% survival rate, that the medical profession was stimulated to consider seriously the possibilities of surgery in the treatment of cardiac disease.

With the introduction of anaesthesia in 1846 by William Thomas Morton,[19] and of antiseptic surgery in 1865 by Lister,[20] who based his work on the clear enunciation by Pasteur[21] of the theory that bacteria were a cause of disease, experimental surgical procedures began to be undertaken on animals. Becker,[22] an ophthalmologist, in 1872, in order to investigate the pulsation of the retinal vessels in aortic incompetence, was able to destroy one or more of the valve cusps experimentally in dogs, by inserting a glass rod down the left carotid artery. Klebs[23] (1875) produced similar lesions using a 'valvulotome'—a tiny knife on a long rod—which he inserted down the carotid arteries, and Cohnheim[24] (1877) using whale-bone sounds, Timofejew[25] (1888) using sounds and needles passed via the aorta and Rosenbach[26] (1889) using the 'valvulotome,' conducted similar experiments in order to study the haemodynamics of aortic regurgitation.

Meanwhile Block[27] in 1882 had successfully sutured lacerations made in the hearts of rabbits. A few years later first Reed[28] (1887) and then Dalton[29] (1891) each successfully repaired a wound of the pericardium and 13 years after Block's successful experiments Del Vecchio,[30] at the meeting of the Eleventh International Medical Congress at Rome in 1895, demonstrated healed wounds of the heart, in dogs, following suture. Within a year Rehn[5] of Frankfort had performed the first successful operation of an human heart (9 September 1896).

Despite the successes obtained during this period, medical opinion was divided on the merits of these newly introduced operations. Billroth,[31] himself no timid surgeon, wrote in 1875: 'Paracentesis of the pericardium is an operation which, in my opinion, approaches very closely to that kind of intervention, which some surgeons would term a prostitution of the surgical art, and others madness'; and again in 1885,[32] 'Let no man who hopes to retain the respect of his medical brethren dare to operate on the human heart.' Later, Riedinger[33] in 1888 wrote: 'The suggestion to suture a wound of the heart, although made in all seriousness, scarcely deserves mention.' and Paget[34] (1896), unconvinced by the demonstration of Del Vecchio in the previous year stated: 'Surgery of the heart has probably reached the limits set by Nature to all surgery; no new methods and no new discovery can overcome the natural difficulties that attend a wound of the heart.'

Others however, were more optimistic. Weill[35] (1895) and Delorme[36] (1898) advocated the surgical treatment of constrictive pericarditis. Tuffier[37] (1897) successfully treated a case of cardiac arrest occurring during chloroform anaesthesia, by massaging the heart.

In 1898, Samways[38] an English veterinary surgeon, first suggested the possibility of incising the mitral valve as a treatment for mitral stenosis and 4 years later Sir Lauder Brunton[39] (1902) published a 'preliminary note on the possibility of treating mitral stenosis by surgical means.'

The ensuing decade produced a vast amount of experimental work on the surgical treatment of valvular deformities. MacCallum and McClure[40] (1906) and Wiggers and du Bois[41] (1913) repeated and elaborated the earlier experiments of Kleb3[23] and Cohnheim.[24] Haecker[42] (Germany) and Cushing and Branch[43] (America) almost simultaneously in 1907 reported the first series of experiments in which valves were cut in animals using a transthoracic approach. These reports were of great value in that they were the first to give hope that with improved techniques the risk of operation could be made almost negligible.

No new suggestions for the relief of valvular lesions were forthcoming until in 1913 Ernst Jeger[44] published his monograph, *Die Chirurgie du Blutgefasse und des Herzens,* in which he suggested the use of venous shunts from the ventricle to the main vessel, as a means of overcoming valvular stenosis. In the same year Doyen[45] (1913) performed the first definitive intracardiac operation on a 20-year-old female patient. His attempt to divide a stenosed pulmonary valve by inserting a small tenotome knife into the right ventricle was unsuccessful, and a post-mortem examination revealed a marked subvalvular narrowing rather than the localized stenosis that had been anticipated. Later that year Tuffier[46] (1913) successfully dilated the aortic ring in a patient with aortic stenosis, by invaginating the wall of the aorta just above the valve, and pushing the wall into the stenosis on the forefinger.

Almost a decade was to pass before a further attempt at surgery on the heart valves was made. In the interim the First World War (1914–1918) provided surgeons with experience in the treatment of wounds of the heart and it became obvious that the heart was able to tolerate manipulation and suturing. Ballance[7] was able to collect from war records 58 case reports; of these cases, 44 recovered. Lockwood,[47] however, considered that many more cases were treated and never reported, 'because of pressure of work, loss of statistics, deaths among surgeons in advanced operating centres and such contingencies.'

The post-war years saw a revival of experimental cardiac surgery and in 1920 Cutler, Levine and Beck[48] commenced an investigation into the possibility of treating mitral stenosis by surgical means. Initial experiments to divide the stenosed mitral orifice under direct vision—by temporarily occluding the great vessels—were unsuccessful, and the operation was abolished in favour of a blind approach through the left ventricle, using small knives on long handles.

In May 1923 Cutler and Beck[49] performed the first operation for mitral stenosis on an 11-year-old female patient. Using a tenotome knife inserted through the left ventricle, an attempt was made to incise each cusp of the obstructing ring. This patient survived for 4½ years but 4 further operations during the next 2 years were unsuccessful.

Meanwhile in 1922 Allen and Graham,[50] of St. Louis, reported a new method of intracardiac surgery, using the cardioscope, an instrument rather like a female cystoscope, which enabled them to visualize the mitral valve. They inserted the instrument through the left auricular appendage, in preference to the left ventricle, the latter route carrying a 50% mortality rate when used in animal experiments. The following year Graham[50] attempted his first clinical case. The cardioscope was inserted into the left auricle, but before any definitive surgical procedure could be carried out, the patient succumbed.

The first successful operation for mitral stenosis at which the fused commissures of the valve were split digitally, was performed by Sir Henry Souttar[51] in 1925. His original intention, to divide the stenosed valve instrumentally, was abandoned during the course of the operation, after he had passed his index finger through the valve orifice without encountering resistance, and to him must go the credit of having performed the first mitral commisurotomy.

Three further attempts at direct valvular surgery were made during the 1920's. Pribram[52] in November 1925 performed the operation of mitral valvotomy on a 28-year-old female patient, using a cardiovalvulotome inserted via the left ventricle, and Cutler and Beck[49] in November 1926 and again in April 1928 attempted to relieve a stenosed mitral valve, also using the cardiovalvulotome; all 3 operations were unsuccessful.

The high mortality rate in these initial direct operations dissuaded surgeons from attempting further operations and no clinical progress was reported for 18 years, until Holmes Sellors[53] and Brock[54] in 1948 first described the technique of pulmonary valvotomy. During the same year Bailey[55] and Brock[56]

successfully performed the operation of mitral valvotomy, thus opening the modern era of direct attack on the heart valves. The previous year Smithy[57] (1947), himself a victim of the disease, had revived interest in the possibilities of the surgical treatment of aortic stenosis, and in the ensuing few years several reports dealing with blind digital and instrumental techniques via the aorta and left ventricle, to fracture or dilate the stenosed aortic valve, appeared in the literature. (Bailey *et al.*,[58, 59] 1950, 1952; Brock[60] 1950; Muller *et al.*,[61] 1954; Swann *et al.*,[62] 1954).

The problem of valvular regurgitation proved more difficult of solution. Some measure of success was achieved by Hufnagel[63] (1951) who described the use of a Lucite ball-valve inserted within the descending thoracic aorta for the correction of aortic incompetence; by Murray[64] (1950), Bailey *et al.*[65] (1951), Davila *et al.*[66] (1954), Sakakibara[67] (1955), Harken[68] (1955), and Glover and Davila[69] (1957) who used various closed techniques for the correction of mitral insufficiency. However, no satisfactory surgical treatment for either of these defects has yet been devised. Recent work however on the correction of aortic incompetence by Barnard[70] (1958), and of mitral incompetence by Kay *et al.*[71] (1958) and by Lillehei *et al.*[72] (1958) holds considerable promise for a 'cure' in the near future.

Following Jeger's[44] suggestion in 1913 to by-pass diseased valves, many attempts have been made to improve cardiac abnormalities by indirect operations. Jarotsky[73] of Moscow (1926) suggested the production of a defect in the atrial septum, to relieve the symptoms of mitral stenosis, his theory being based on the belief that patients with Lutembacher's syndrome have a better prognosis than those with pure mitral stenosis. Bailey[74] (1950) performed such an operation; the patient died 60 hours after operation due to the inability of the heart to maintain an adequate left ventricular output.

Swan[75] (1949) performed pulmonary-azygos vein anastomosis in the dog as a means of relieving pulmonary congestion in mitral stenosis. He believed, however, that a reduction in left arterial pressure would decrease left ventricular filling and hence left ventricular output, so he did not perform the operation of humans. In the same year Sweet and Bland[76] performed this operation 6 times. There was one fatality and the remaining 5 patients were regarded as being appreciably relieved.

In an attempt to achieve the same object, Cossio and Perianes[77] (1948) anastomosed the left inferior pulmonary vein to the splenic vein, but the anastomosis did not remain patent. In order to decrease right ventricular output, and thus relieve pulmonary congestion, they produced tricuspid incompetence (initially in dogs and later in 5 patients) by inserting a hooked instrument via the internal jugular vein, but the results were poor, only one patient being improved. Ligation of the inferior vena cava, the ligature being placed below the renal veins, was also attempted, with some success (Cossio and Perianes[78] 1949), and in 1951 Donzellot[79] reported 38 cases, of which 16 were markedly and 11 slightly improved. Bill, Pierce and Gross[80] (1950) and Marcus[81] (1951) attempted unsuccessfully to by-pass the mitral valve by means of grafts and prostheses from the left auricular appendage to the left ventricle; Rappaport *et al.*[82] (1948) performed a direct anastomosis between the left auricular appendage and the left ventricular cavity, and more recently Hufnagel *et al.*[83] (1954) and Sarnoff and Case[84] (1955) have revived interest in attempting to by-pass the arctic valve.

Advances in the treatment of congenital cardiac abnormalities had been proceeding apace. Munro[85] in 1907, first suggested that cases of patent ductus arteriosus should be treated by ligation of that structure, and Graybiel *et al.*[86] were the first to attempt the operation in 1938. The following year Gross[87] (1939) reported the first successful ligation and in 1947[88] recommended the present-day method of treatment—that of excision and ligation. Crafoord[89] and Gross,[90] independently during 1948, introduced the surgical correction of coarctation of the aorta. The same year Blalock and Taussig[91] (1945) introduced their operation of systemic-pulmonary artery anastomosis for the treatment of the tetralogy of Fallot; the following year Potts[92] (1946) suggested the easier operation of aortic-pulmonary artery anastomosis, and two years later Brock[54] performed the physiologically sounder operation of pulmonary valvotomy.

Murray[93] (1948), by introducing a strip of fascia lata into the right ventricle and attaching it to the septum, repaired an interventricular septal defect in Man after animal experiments had demonstrated its possibility. He also first described a technique of closure of interatrial septal defects, by passing sutures through the anterior wall, beginning to the right of the aorta and the pulmonary artery, to emerge posteriorly between the superior vena cava and the right pulmonary veins. The sutures were tied posteriorly, thus compress-

ing the anterior and posterior walls of the atria. Cohn[94] (1947), Swan *et al.*[95] (1950 and Santy *et al.*[96] (1950) devised methods for invaginating the atrial appendage or the lateral wall of an auricle to occlude a septal opening, and Gross *et al.*[97] (1952) described the use of a rubber 'atrial well' in order to correct such a defect.

Despite the advances which had been made by the middle of the 20th century, the cardiac surgeon was still hampered by his inability to visualize the operative field. The dangers and uncertainties of blind instrumentation and digital manipulations were realized and a suitable technique to allow of visualization of intracardiac lesions was sorely needed. This was soon accomplished by the use of general hypothermia and inflow stasis (Bigelow *et al.*,[98] 1950; Delorme,[99] 1952; Ross,[100] 1954; Gray,[101] 1955; Swan and Blount,[102] 1956) and in 1952 Lewis[103] performed the first open heart operation—the closure of an inter-atrial septal defect.

Numerous techniques for the induction of controlled hypothermia, including drugs, surface cooling, vascular cooling, internal cooling or a combination of two or more of these were then employed clinically. The complications of hypothermia,[118] however, are many and the time limit when using this technique is such that only relatively simple abnormalities such as septal defects and stenotic valvular lesions can be corrected. In order to repair more complicated anatomical abnormalities the heart must be excluded from the circulation for a longer period of time, and with this aim in mind surgeons continued to search for a method which would allow them prolonged access to the open heart.

Success was not long in coming and in 1953 Gibbon[104] performed the first successful open heart operation using a pump oxygenator. The heart and lungs were excluded completely from the patient's circulation for 25 minutes, and an interatrial septal defect was repaired. Two years later Melrose *et al.*[105] (1955) advocated the use of potassium citrate for inducing cardiac arrest, thus enabling the surgeon to work within a still, dry heart. The following year Effler *et al.*[106] (1956) first employed the Melrose technique clinically, Lam[107] (1956) reported on the use of acetylcholine as a cardioplegic agent, and Lillehei *et al.*[108] (1956) developed the technique of retrograde coronary sinus perfusion for direct vision surgery of the aortic valve.

Since the advent of extra-corporeal oxygenation two basic systems have proved successful in clinical application. In the one group are the biological oxygenator systems employing cross-circulation (Lillehei *et al.*,[109] 1955; Warden *et al.*,[110] 1954), heterologous (dog) lungs (Campbell *et al.*,[111] 1955), or a reservoir of oxygenated blood (Warden *et al.*,[112] 1955). In the other group are the artificial oxygenators employing one of three basic methods for extra-corporeal arterialization of venous blood. These are:

1. The bubble oxygenator, in which oxygen is introduced directly into the venous blood (DeWall *et al.*,[113] 1956);

2. The film oxygenator, in which the red cells are also exposed directly to oxygen by being spread in thin layers over a large surface (Miller and Gibbon,[114] 1951; Gross,[115] 1956);

3. The membrane oxygenator, in which oxygen and venous blood are exposed over a large surface separated by a suitable membrane, such as cellulose, which is permeable to oxygen and carbon dioxide (Kolff *et al.*,[116] 1956).

The interior of the heart, so long an important barrier to progress and the last anatomical difficulty of the many that have confronted surgeons through the ages, has finally been conquered utilizing one of these methods of extra-corporeal oxygenation. Many complex cardiac lesions, until a few years ago considered to be incurable, are now being treated surgically every day in centres throughout the world. It remains for surgeons in the future to improve upon the methods of the present, and to devise new operations and techniques in order to repair those lesions which are to-day still incurable. As we progress, indirect procedures which can only, at best, bring about symptomatic improvement must be replaced by operations which restore structural and functional normality. In the words of Sir Russel Brock[117] in an address before the Henry Ford Hospital International Symposium on Cardiovascular Surgery in March 1955, 'The future of all cardiac surgery must turn more and more toward direct and away from indirect surgery.'

OPSOMMING

Die jongste vorderings op die gebied van hartchirurgie in Suid-Afrika het 'n nuwe tydperk in die geskiedenis van die geneeskunde in ons land ingelui. Hierdie vorderings is moontlik gemaak deur die prestasies van talle werkers van talle verskillende nasionaliteite dwarsdeur die wêreld, en om die merkwaardige vooruitgang wat hierdie vertakking van die chirurgie in die afgelope paar jaar gemaak het, toe te lig, word die ontwikkeling van hartchirurgie

vanaf sy primitiewe aanvang tot die gevorderde stadium wat dit tans bereik het, geskets.

Dwarsdeur die eeue is groot klem op proefondervindelike werk gelê, en die belangrike eksperimentele ontdekkings van die verlede, asook die mylpale in kliniese prestasies, word verduidelik.

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ORAL IMMUNIZATION AGAINST COLDS

A PRELIMINARY REPORT

D. J. MESKIN, M.B., B.CH. (RAND)
Johannesburg

Most of the work on vaccine prophylaxis and treatment of colds and upper respiratory infections was done before the advent and extensive use of antibiotics. Study of the medical literature reveals that interest in problems of immunity in infectious diseases was overshadowed by the investigation of antibiotics. In recent years, with the realization of the limitations of antibiotic therapy, investigators have again turned to the study of immunity.

Historical. Absorption of bacterial antigens from the alimentary tract and subsequent

manifestations of immunity were observed by early investigators.[1-6]

Oral immunization against colds and upper respiratory tract infections was successfully applied by several investigators. Cronin Lowe[7-8] published short reports on his observations in 1932 and 1936. Rockwell *et al.*[9] in 2 successive years orally immunized 500 and 448 persons with a vaccine containing streptococci, pneumococci, *H. influenzae* and *M. catarrhalis*. They obtained a decrease of 45% and 44% respectively in the incidence of colds when the results were compared with their control groups.

Several trials on a large scale were conducted in the U.S.A. to establish the value of prophylactic oral immunization against colds. The vaccines used were prepared in the same way as Rockwell's, but staphylococci and *Bact. mucosus capsulatus* were added. A study was carried out at one of the industrial plants for 2 successive years. It was found that whereas hypodermic immunization was successful in 63%, oral administration of the vaccine was effective in 80% of the treated persons.[10] In another plant large-scale oral immunization was found effective in 88% of all immunized persons.[11]

Stafford,[12] in a carefully controlled study on 338 students of the Miami University, showed that whereas the incidence of mild colds did not significantly diminish, the occurrence of severe colds was strikingly less in the immunized group. An epidemic of very severe colds broke out during the season and it was recorded that the immunized students enjoyed almost complete protection.

JOHANNESBURG TRIAL

A trial was conducted in an attempt to establish whether oral immunization before the beginning of the winter season would reduce the incidence of colds. Employees of the Municipal Electricity Department were advised that a limited amount of vaccine was available for distribution. Many volunteered but 200 were selected who, according to their histories, had been suffering from recurrent, moderate or severe colds in previous years.

It was impossible to obtain accurate data concerning the number and symptoms of the colds and the organs affected. Consequently their statements had to be accepted and throughout this study the main criteria were the number and severity of the colds in previous years and during the autumn to spring season of 1958, as reported by the persons who took part in the trial.

Before issuing the vaccine every person was interviewed and care was taken not to influence them in any way. All statements were volunteered without prompting on the part of the interviewer.

The vaccine* used in this trial contained in each dose:

Pneumococcus Types I, II and III, 3,000 million organisms; *Streptococcus haemolyticus*, 2,000 million organisms; *Streptococcus viridans*, 2,000 million organisms; *Staphylococcus aureus*, 400 million organisms; *Haemophilus influenzae*, 2,000 million organisms; *Bact. mucosus capsulatus*, 600 million organisms; *Micrococcus catarrhalis*, 1,000 million organisms.

In addition to the bacterial bodies the vaccine contained staphylococcus toxoid in each dose. Thus the vaccine differed from that used by other investigators by virtue of the added toxoid. This seemed advisable because of the great increase in the incidence of stapyhlococcal disease in recent years, the experience that staphylococci were the predominating organisms in respiratory infections and because it is now recognized that the exotoxins are of greatest importance in the establishment and spread of staphylococcal infections.[13-16]

The vaccine was in the form of sublingual tablets and the persons taking part in the trial were instructed to take one tablet twice daily. They were told to place the tablets under the tongue and to allow them to dissolve without chewing or sucking. This method of administration is preferable to swallowing because absorption of bacterial antigens and toxoid is greater and more regular from the sublingual and oral mucous membrane than from the gastrointestinal tract.[17, 18]

Each person was given 24 tablets in mid-April and interviewed again in November. The information was given freely and the writer feels that it was unbiased because municipal employees get paid sick leave and stood to gain nothing by attending daily.

Of the 200 volunteers, 103 completed the prescribed course and answered the questionnaire. Six persons took a certain number of tablets and did not complete the course. These are not included in the report. Because of transfers to other branches, change of employment and other causes, 91 were lost to follow up.

Results. The volunteers were classified in 4 groups as having had in previous years:

i. Occasional moderate colds;
ii. Occasional severe colds;
ii. Frequent moderate colds;
iv. Frequent severe colds.

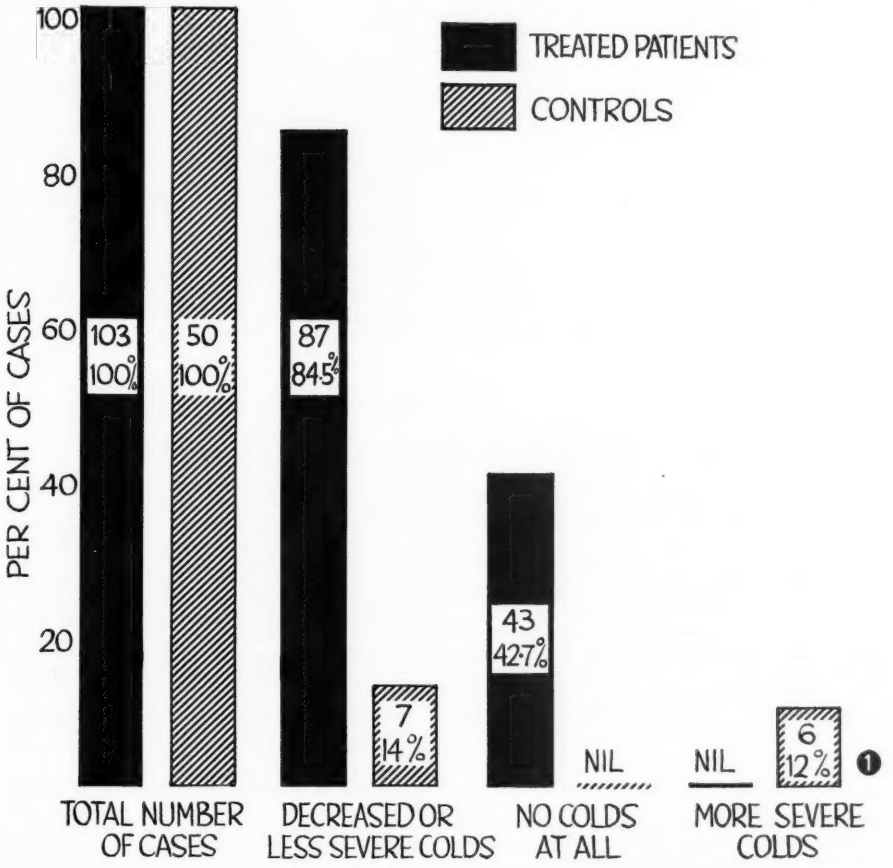
* Imuvac tablets supplied by Saphar Laboratories Ltd., Johannesburg.

Sixteen persons (15.5%) reported that they had not benefited from the vaccine treatment. The number and the severity of the colds were about the same as in previous years. The failures were approximately evenly distributed in the 4 groups.

Eighty-seven persons (84.5%) reported that they undoubtedly benefited from the immunization, 43 having had no colds at all during the autumn or spring season following immunization. The remaining 44 persons stated that they had benefited by the vaccine treatment but had had occasional colds; 28 had only one bout during the season, 14 had two or more but these attacks were considerably less severe than in previous years. Two persons reported that although the number of colds did not appreciably diminish, these were milder and of shorter duration than in previous years.

Of the 44 persons who had one or more colds, 37 stated they were milder, less troublesome and of shorter duration. Ten reported that they repeatedly or occasionally felt the prodromal symptoms which usually heralded the beginning of a cold, but these subsided and no cold developed. Several persons who used to suffer from occasional or frequent severe colds reported that this was the first winter in many years that they had been cold-free. Two of them added that all the members of their families had the usual winter colds and that they alone remained unaffected. One person reported improvement in chronic sinusitis.

In order to establish whether the benefit that these 87 persons derived from the immunization was real or only apparent, and whether the seasonal colds of 1958 were generally of a milder nature, 50 persons who had received no



vaccine were interviewed and questioned about the incidence and severity of their colds that season. Seven stated that they had had fewer colds than in previous years. Six had had more frequent and more severe colds than before. Thirty-seven had had about the same number of colds, and these were as severe as in past years.

COMMENT

The number of participants in this trial was small and so one was hesitant to limit the number of persons treated by using the double-blind control technique. With the small control, however, making allowance for the 14% who had fewer colds than in previous years, approximately 70.5% benefited from the prophylactic treatment (Fig. 1).

Since compiling this report preparations are being made to repeat this trial on a further 300 volunteers using the double-blind technique. There have been many enquiries from last year's participants, who wish to repeat the oral vaccine prophylaxis. Having used a vaccine containing staphylococcal toxoid for the first time, and in view of recent publications on the toxoid, one feels that there is much scope for investigation in that direction.

SUMMARY

1. A preliminary report on the use of oral vaccine prophylaxis against colds is submitted.

2. There was undoubted benefit in 84.5% of persons, which compares favourably with results obtained by overseas workers.

I wish to thank Dr. A. Janovics, of Saphar Laboratories Ltd., Johannesburg, who made this trial possible by supplying the vaccine, and for his invaluable advice and help.

Thanks must also go to Mr. F. Palmer of the Electricity Department, Johannesburg, at whose suggestion this trial was undertaken, for his untiring work with the volunteers.

OPSOMMING

'n Voorlopige verslag oor die gebruik van 'n mondelinge entstof vir die profilakse van verkoues word voorgelê.

84.5% van die persone het ongetwyfeld by die behandeling gebaat. Dit vergelyk gunstig met die resultate wat deur navorsingswerkers in die buiteland behaal is.

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NOTES AND NEWS : BERIGTE

Mr. Wilfred Kark, F.R.C.S. of Johannesburg, is leaving shortly for a 2-month visit overseas. He will visit clinics in Europe and in England.

• • •

6TH INTERNATIONAL CONGRESS FOR INTERNAL MEDICINE

This will be held in Basel (Switzerland) from 24–27 August 1960. It will be organized in conjunction with the Swiss Society for Internal Medicine.

For further details please apply to the Secretariat of the 6th International Congress for Internal Medicine, 13 Steinentorstr., Basel.

• • •

A NEW FILM ON DERMABRASION

Westdene Products (Pty.) Limited announce that a new film *Laboratory-Pharmacology and Dermabrasion Technic* has been added to their library and will be loaned on application to their Public Relations Department, P.O. Box 7710, Johannesburg.

The film has been produced by the S. E. Massengill Company, U.S.A., in co-operation with Mr. G. Fulton, Ph.D., Boston University, and Dr. H. J. Bernhardt, Dermatologist. The film, which is in colour, is for use on a 16 mm. sound track projector, and runs for 10 minutes. It is a vivid demonstration of the 'before and after'—'with and without' application of Adrenosem. This is presented in a pharmacological animal study and a dermabrasion surgical procedure.

The film is in two parts—*Part 1*: Pharmacology. A hamster cheek pouch is used to show the capillary system and Adrenosem action. *Part 2*: Dermabrasion (steel-brush technique) procedure. Surgery is performed on one side of the face *without* preoperative use of Adrenosem and on the opposite side *with* Adrenosem. Blood loss is minimized, the operative field is clearer and there is less patient discomfort with the use of Adrenosem.

Dr. Norman Klass has left for 3 months post-graduate study in Israel, Europe and England and will return at the end of June.

His practice is being carried on in his absence with the kind assistance of the other local specialists in Physical Medicine.

* * *

ULCERATIVE COLITIS

Protea Pharmaceuticals Ltd., P.O. Box 7793, Johannesburg, are preparing to mail a series of medical journal abstracts on *Ulcerative Colitis* to all those interested.

There are 6 different sets, the first of which will be sent out in the very near future. *These abstracts will be supplied absolutely free of charge.*

When making a request, please ensure that your signature is legible and that your address is included.

* * *

WELLCOME RESEARCH TRAVEL GRANTS

REGULATIONS

1. The awards are known as Wellcome Research Travel Grants, and are open only to workers who are themselves engaged in research on problems of human and animal medicine, or in such related fields of experimental science, as the Trustees shall interpret as falling within the terms of the Will of the late Sir Henry S. Wellcome. Attendance at meetings of a professional as opposed to a scientific nature and travel undertaken purely for educational purposes cannot be subsidized.

2. The awards are made by the Wellcome Trustees on the basis of the information provided by the candidate, and with due regard to the support given to his proposal by the authority recommending him. The question whether an applicant is eligible for a grant will, however, be a matter entirely for the Trustees' discretion.

3. The duration of the short-term awards may range from the few days which may be all that are necessary for consultation with colleagues in other countries about the progress of research on a common problem, or for attendance at a scientific meeting, to the period of weeks or months that may be needed either to acquire a new research technique or to undertake an investigation at a centre overseas where the facilities for it are likely to be particularly good. Grants for both travelling and subsistence expenses will not normally be made in respect of a longer period than six months. Candidates wishing to consult with colleagues abroad, or to work at a research centre overseas, should find out in advance that their visits will be acceptable to the colleagues in question (including, of course, the director of any research centre to be visited), and should mention this in their applications.

4. The value of the grants for subsistence will ordinarily be computed on the basis of the allowances made to U.K. public servants of equivalent standing paying official visits of similar duration to the country and town(s) in question. Information about the current rates of these allowances, which vary greatly from place to place and from time to time, will be obtained on request for candidates whose applications are suitably supported. In completing the application form the candidate is invited to state his own estimate of the cost of the visit, but any award made to him would be subject to adjustment in the light of the latest information about the rates allowed for public servants. Where the cost of the visit would be partly provided from another source (other than the candidate's own pocket) the value of the grant made would be subject to modification.

5. The awards take the form of *block grants*, paid normally in advance, to cover the candidate's return fare and the approved rate of subsistence (where this is provided). Successful candidates will not be required to account for the expenditure if the visit duly takes place as planned, and is of the duration sanctioned. Should the candidate's journey, or the duration of his visit, be curtailed for any reason, he will be expected to refund to the Trustees an appropriate proportion of the grant. Any proposal to modify the visit, after the grant has been made, will be subject to the Trustees' approval, and application for permission for any such alteration of programme must be made to the Deputy Scientific Secretary of the Trust before the change is undertaken.

6. The provision for travelling expenses will normally cover the candidate's railway and steamship fares, including berths, it being understood that travel shall be by the shortest practicable routes. Tourist class air travel may be allowed in the case of short visits and where there is no substantial difference from the cost of steamship fares, or where there are special reasons of urgency.

7. In the case of the system of short-term awards (for visits up to six months in duration) no provision can by made by the Trustees for the travelling or subsistence expenses of the wife or family of a candidate, and unless the candidate has independent financial resources sufficient to cover the additional expenses, it is expected that his family will be left at home. In the case of visits expected to last for a year or more (where travelling expenses only are to be provided), the Trustees may be prepared in suitable circumstances to consider making a contribution to the cost of travel for a married candidate's wife and family.

8. Recipients of Wellcome Research Travel Grants are expected to make their own arrangements for travel and accommodation, and to obtain their own passports, visas and tickets. They should also make their own arrangements, through their Banks, to obtain the necessary foreign currency. Where difficulty is encountered in obtaining dollars for a projected visit to the U.S.A. or Canada, the advice of the Deputy Scientific Secretary may be sought, in case it should be possible for the Trust to assist.

9. Since the object of the Wellcome Research Travel Grants is to provide travelling, subsistence and incidental expenses only (and not stipends or other personal emolument) they do not rank as income for the purpose of the U.K. Income Tax Acts and need not be returned as such.

10. On completion of the period of a Wellcome Research Travel Grant, the recipient should submit a brief report of his visit, in the form of a letter to the Deputy Scientific Secretary of the Trust. The fact that a Wellcome Research Travel Grant was made in respect of it should be mentioned in any scientific publication directly resulting from the visit.

The Chairman of The Wellcome Foundation Limited and former British atomic research scientist, Mr. Michael W. Perrin, toured the Union recently from Britain during his survey of Africa south of the Sahara.

He is here seen (right) with Mrs. Perrin, Advocate Bertha Solomon, retired M.P. and specialist in women's rights and social welfare, and Prof. R. A. Dart, formerly Professor of Anatomy at the University of the Witwatersrand, at a reception given at the Carlton Hotel, Johannesburg, by Burroughs Wellcome and Company, in honour of Mr. and Mrs. Perrin.

PREPARATIONS AND APPLIANCES

PEROLYSEN TABLETS

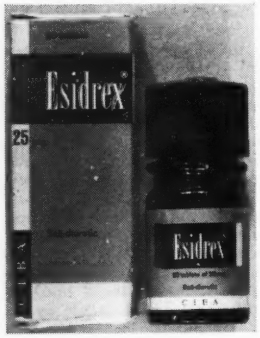
Maybaker (S.A.) (Pty.) Ltd. wish to announce that in addition to 5 mg. and 10 mg. tablets, a 1 mg. presentation of *Perolysen* brand pempidine tartrate is now available.

Perolysen is an oral ganglion blocking agent indicated in the management of selected cases of hypertension, particularly severe essential, and malignant hypertension. Because increases in dosage of pempidine of the order of 1 mg. have proved significant, it is considered that a tablet of this strength will be useful in clinical practice.

ESIDREX*

HYDROCHLOROTHIAZIDE

This is a product of original Ciba research, being a potent oral sali-diuretic well indicated in the treatment of hypertension, toxaemias of pregnancy and oedema of varying origin.



It potentiates the action of antihypertensive agents such as Serpasil*, Apresoline*, Nepresol*, Adelphane* and ganglionic blockers and because of its marked effect on sodium chloride excretion permits less severe dietary restrictions of salt intake.

Because of its only slight influence on potassium excretion, risk of hypopotassaemia is low but during prolonged *Esidrex* therapy additional potassium (1–3 g. potassium chloride daily by mouth) should be given.

Dosage: Initial daily dosage 25 to 75 mg. and an average of 25 mg. daily, depending on individual requirements for maintenance.

Packages: Tablets of 25 mg. in bottles of 20 and 100.

* T.M. Regd.

REVIEWS OF BOOKS

THE LIPIDOSES

Lipidoses. Diseases of the Intracellular Lipid Metabolism. Revised and edited by Siegfried J. Thannhauser, M.D., Ph.D. 3rd ed. (Pp. 590+Index. Illustrated). New York: Grune & Stratton.

Everybody who is interested in the problems arising from disturbances of lipid metabolism is acquainted with Thannhauser's previous monographs on this subject. It is now 8 years since the 2nd edition was published and, as the author says, since this time there have been significant advances in both the chemical and clinical aspects of the problem.

The present edition deals exhaustively with the physiology and chemistry of lipid metabolism, with hyperlipaemia, the xanthomatoses, Gaucher's disease, Niemann-Pick disease, infantile amaurotic idiocy and gargoylism. Each section is accompanied by a full bibliography, and in the clinical chapters there are many examples of typical cases.

Thannhauser has now modified his concept of xanthomatous biliary cirrhosis and is satisfied that the xanthomatous manifestations are secondary to a primary biliary cirrhosis. This has clarified that particular problem. It is refreshing also to see that the author in his discussion on hypercholesteraemia emphasizes that blood vessels are not only a system of tubes for blood transport but are themselves organs with complex metabolic functions; and that they may be active in the production of atherosclerosis and not merely passive participants.

The new edition is now fully up-to-date and a valuable reference work. One small criticism emerges—the quality of some of the illustrations could have been improved.

EPILEPSY

Epilepsy Handbook. By Frederic A. Gibbs, M.D., and Frederick W. Stamps, M.D. (Pp. 92+Index. With 9 Figs. 36s.). Oxford: Blackwell Scientific Publications.

In 101 pages the authors from the University of Illinois, Chicago, have produced an excellent handbook on epilepsy.

They stress the value of the clinical history, giving a life 'recording' in contrast to the electroencephalograph which is but an hour's 'recording' of the cerebral pattern. As epilepsy is an intermittent disturbance of cerebral rhythm, its value is limited. Also therapeutic response does not necessarily depend upon the EEG findings.

A short chapter is devoted to each type of epilepsy. The clinical features are discussed as is the type of therapy recommended. All the closely related non-epileptic seizures are separately reviewed and differentiated.

In the second half of the book each therapeutic agent is again discussed, its indications and side effects being underlined.

In the frontispiece is an excellent coloured reproduction of all the drugs commonly used.

The book is short, concise, easily readable and an essential book for every practitioner. The doctor is clearly told what is wrong and how it can be treated. Theoretical discussion and references are kept to a minimum and only the practical clinical features are stressed.

GADDUM'S PHARMACOLOGY

Pharmacology. By J. H. Gaddum, M.R.C.S., L.R.C.P., Sc.D., F.R.S. (Pp. xvi + 587, 5th ed., 42s.). London and Cape Town: Oxford University Press. 1959.

This textbook, first published in 1940, was an original conception designed to present general principles in pharmacology and the kind of evidence that justifies the trial of new drugs. The author is well known as a distinguished medical scientist whose name is connected with technical methods, experimental procedures and theories that are basic to research work in pharmacology, physiology and biochemistry.

This edition is almost 25% larger than the first edition. This is not surprising considering the vast increase in pharmacological knowledge and the very large number of new drugs introduced in recent years. All important drugs in the British Pharmacopoeia (B.P.) 1958 and the U.S.P. 1955 are mentioned in the book; also many nonofficial drugs, and all doses in the metric system as now recommended in the B.P. The largest new sections deal with the methods used in the study of the effects of drugs on the brain, and with radio-active isotopes. Many other changes have been made. There are many tables, figures and illustrations.

The book is most readable and of great value to medical students, especially those in the preclinical stage, but also to medical men who investigate the effect of new drugs on patients.

The author states that the purpose of this book is not only to give the essential facts about the drugs used in therapeutics, but also to serve as an introduction to a romantic science which now has intellectual attractions, fertile relations with the sister sciences and practical applications in clinical medicine, veterinary medicine and pest control.

CARCINOMA OF THE LUNG

Neoplastic Disease at Various Sites. General Editor: D. W. Smithers, M.D., F.R.C.P., F.F.R. *Vol. 1: Carcinoma of the Lung.* Edited by J. R. Bignall, M.D., M.R.C.P. 1958. (Pp. 292 + Index. With 59 Figs. 55s.). Edinburgh and London: E. & S. Livingstone Ltd.

This volume is largely concerned with the statistical data compiled from studies of the incidence, etiology, pathology and treatment of carcinoma of the lung. The mortality rates for males and females in England and Wales, which are very low until the third and fourth decades, thereafter rise with each year of the life span. All the evidence suggests that there has been a true rise in incidence, more apparent in males than in females.

It is admitted that the cause of carcinoma of the lung is not yet known, and that the cause of death is frequently obscure except in cases of haemorrhage or proved cerebral metastasis. The crude death rate from carcinoma of the lung has increased nearly 50 times in the last 50 years. A causal specific risk has been established in 5 separate industries. Thus a high incidence has been shown in workers engaged in the mining of certain radio-active ores, refining of metal, the production of gas and the manufacture of chromates and asbestos.

A long chapter deals with the association of tobacco smoking and the production of lung cancer. The authors definitely conclude that cigarette smoking is an etiological factor though they admit that the picture is incomplete. Statistics also support the relationship of atmospheric pollution to the incidence. Non-industrial radio-activity, respiratory infections and heredity do not appear to be of significance.

All primary carcinomas must arise from the epithelium of the bronchi, bronchioles or mucous glands, and the circumferential infiltration proceeds too rapidly for encapsulation. Microscopic section from most cases show the growth of the neoplastic process to be in advance of the apparent edge. The importance of this is emphasized in the statistical study of the results of treatment. The spread of the growth appears to be predominantly by the lymphatics. Statistics show that carcinoma appears to occur a little more frequently in the right lung and in the upper rather than the lower lobes. Routine mass radiography may lead to some early diagnoses, but early cases are not always detected. Some unusual manifestations are discussed.

Certain principles govern the surgical treatment. Radical removal of the growth and the related lymph node area must be performed, though it is important to conserve uninvolved lung. Lobectomy, as opposed to pneumonectomy, palliative resection and radio-active gold grain implantations are discussed. The status of surgical treatment is not a happy one, and the curative potential of radiotherapy for bronchial carcinoma has still to be determined. Supervoltage irradiation has clearly an important place in treatment. Numerous examples are quoted which suggest that a joint attempt by surgeons and radiotherapists should be made to improve the prospects for those comparatively few patients for whom there is a chance of cure by the use of local treatment.

There is a chapter on palliation which points out that cough, pain, haemoptysis, dyspnoea, dysphagia and superior mediastinal obstruction may be relieved by radiotherapy.

A short chapter discusses treatment with nitrogen mustard. A section on the mortality rates over different periods concludes this volume. Numerous graphs and Tables in this worth-while book are of interest to all those concerned with the vexed problem of the etiology, diagnosis and treatment of lung carcinoma.

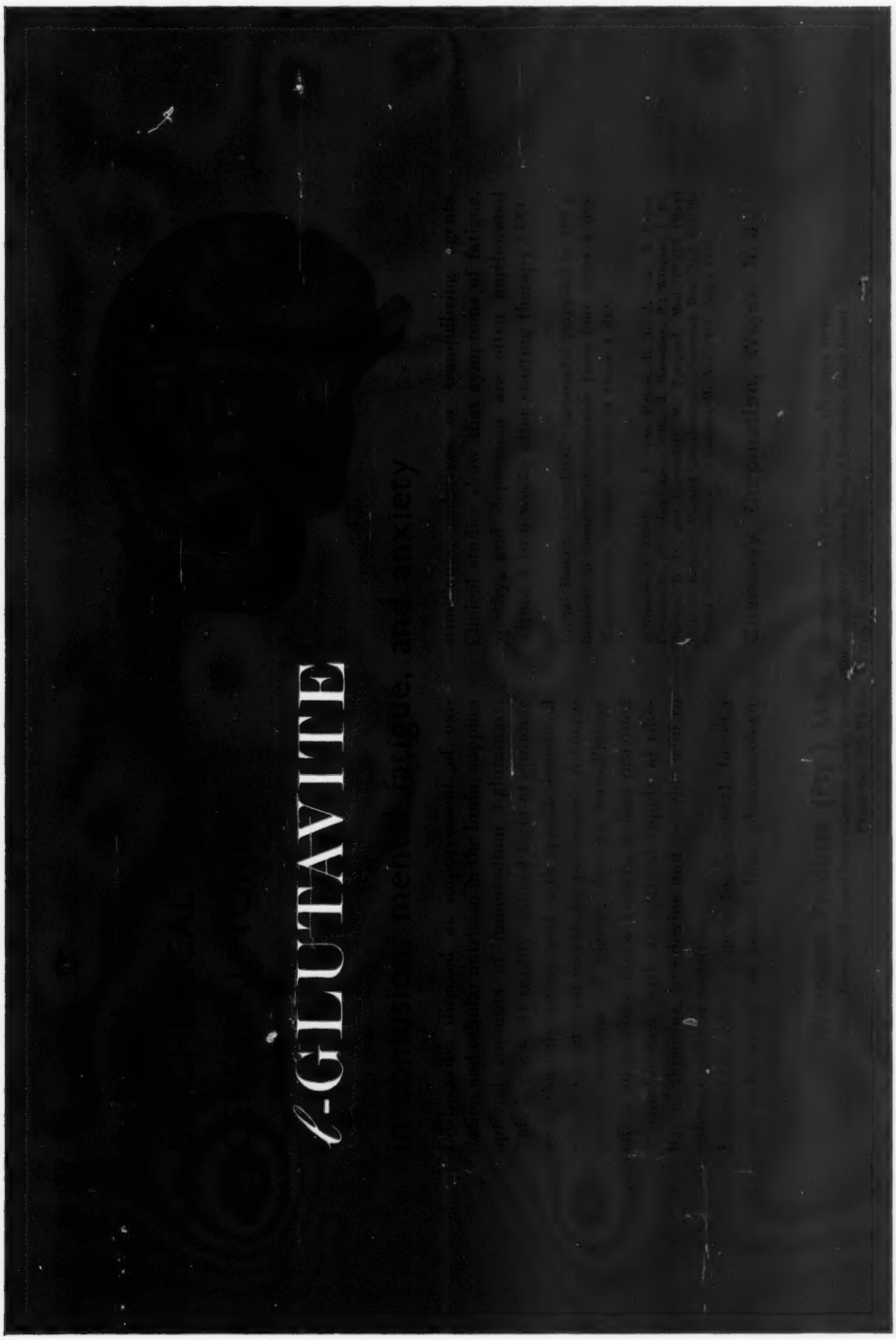
PHARMACOLOGY

Experimental Pharmacodynamics. By T. Koppanyi and A. G. Karczmar. 1958. (Pp. 258. With Figs. $5.50). 2nd ed. Minneapolis: Burgess Publishing Company.

This book is an up-to-date laboratory manual in pharmacology giving details of preparation and procedure for some hundred experiments and demonstrations.

Each set of experiments is preceded by a theoretical analysis of the group of drugs dealt with in that section and is followed by a discussion on 'clinical bearings.'

Although the main usefulness of this book is as a text for a practical course in Pharmacology, the short pithy discussions on the theoretical aspects of the subject could form a useful source of reference on the action and use of drugs.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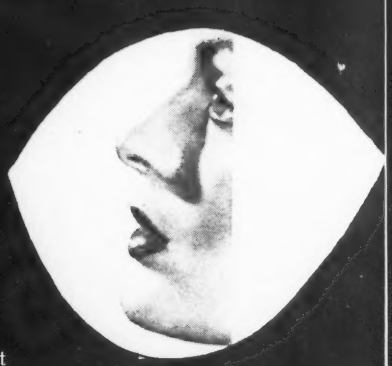

Clinical Effectiveness and Versatility
Rapid Relief—in minutes
Enduring Relief—for hours

Excellent results have been reported[1-4] in over 94 per cent of 1058 cases with nasal congestion due to nasal allergies, sinusitis, the common cold, and a variety of other causes. Most patients—including adults and children of all ages—responded immediately to the first instillation of TYZINE, and decongestive action was noted as lasting four to six hours or longer after a single administration.

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Among the more than 2400 cases recorded in preliminary and published studies, rebound engorgement was virtually absent. Typical of all reports: "The appearance of refractoriness after frequent and prolonged use was not observed."[1] Further, TYZINE maintains or rapidly restores normal physiologic functions of the nose, including ciliary motion and an acid pH hostile to secondary bacterial invasion. Indeed, "In addition to symptomatic relief, it was determined that the use of the decongestant shortened the usual course of each disease, and, additionally, either prevented or aborted complications."[2]

Tyzine*

brand of tetrahydrozoline hydrochloride

"a new and superior topical vasoconstrictor"

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